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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/610,935	07/06/2000	Brian W. Ward	SGM 6934.1	5148

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EXAMINER	
SISSON, BRADLEY L	

ART UNIT	PAPER NUMBER
1634	

DATE MAILED: 08/11/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/610,935	WARD ET AL.	
	Examiner	Art Unit	
	Bradley L. Sisson	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 May 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *13-16,20-22,42-53 and 60-65* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *48-53* is/are allowed.

6)☒ Claim(s) *13-16,20,42-47 and 60-65* is/are rejected.

7)☒ Claim(s) *21 and 22* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114 was filed in this application after appeal to the Board of Patent Appeals and Interferences, but prior to a decision on the appeal. Since this application is eligible for continued examination under 37 CFR 1.114 and the fee set forth in 37 CFR 1.17(e) has been timely paid, the appeal has been withdrawn pursuant to 37 CFR 1.114 and prosecution in this application has been reopened pursuant to 37 CFR 1.114. Applicant's submission filed on 24 May 2004 has been entered.

Claim Objections

2. Claims 21 and 22 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 13-16, 20, 42-47, and 60-65 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled

in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Attention is directed to the decision in *University of Rochester v. G.D. Searle & Co.* 68 USPQ2D 1424 (Fed. Cir. 2004) at 1428:

> To satisfy the written-description requirement, the specification must describe every element of the claimed invention in sufficient detail so that one of ordinary skill in the art would recognize that the inventor possessed the claimed invention at the time of filing. Vas-Cath, 935 F.3d at 1563; see also Lockwood v. American Airlines, Inc., 107 F.3d 1565, 1572 [41 USPQ2d 1961] (Fed. Cir. 1997) (patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention"); In re Gosteli, 872 F.2d 1008, 1012 [10 USPQ2d 1614] (Fed. Cir. 1989) ("the description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed"). Thus, an applicant complies with the written-description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." Lockwood, 107 F.3d at 1572.

5. For convenience, claim 60 is reproduced below.

> 60. (new) An aqueous reagent for use in forming a polymerase reaction mixture comprising a thermostable DNA polymerase, a nucleic acid polymer template, a primer, nucleotides, a detectible anionic tracer dye unbound to primer or nucleotides, and a solute to increase the physical density of the reagent, the reagent comprising the thermostable DNA polymerase, the detectible anionic tracer dye, and the solute but being substantially free of the primer and the nucleic acid polymer template, the reagent having an optical density of about 5 to about 500 at a visible wavelength of maximal tracer absorbance and a physical density of at least about 1.01 gm/cm^3, but less than the density of the solute.

6. Claims 13-16, 20-22, and 60-65 are drawn to a "an aqueous reagent for use in forming a polymerase reaction mixture." Claims 42-47 are drawn to "[a]n aqueous reagent for *ex-vivo* polymerase reaction in which a nucleic acid polymer product complementary to a nucleic acid polymer template is prepared."

7. The specification has been found to set forth but two examples:

- Example 1, pages 18-30, "Identification and formulation of a Taq DNA polymerase with tracers and high density reagent," sets forth a preferred embodiment (see page 29). In Example 1, it is disclosed that"[f]rom 180+ red dyes (absorbance max between 450 and 570 nm) (Table 1)" but 6 dyes (Bordeaux 1, Acid Red 106, Acid Red 4, Acid Red 1, Amaranth, and Acid Violet 97) have been found to be compatible with Taq polymerase.
- Example 2, pages 30-31, "Determination of the compatibility of a dye with restriction endonuclease."

As presently worded, the reagent of claims 13-16, 20-22, and 62-65 comprise DNA polymerase and an anionic tracer dye, be "substantially free of the primer and the nucleic acid template" and have an optical density from about 5 to about 500. Table 1, found at pages 19-23, provides a listing of "Dyes initially considered", have maximal absorbance from 430 to 617. Page 25, first paragraph, states that of the listing of "dyes initially considered," only 20 were evaluated. Page 26, first paragraph, states that PCR toxicity was observed for some of the 20 dyes examined and were eliminated from the group of suitable dyes. Page 27, second paragraph, states that desalted dyes were less toxic as compared to crude dyes, and that ammonium salts of the dyes were the most toxic. As presently worded, the claimed compositions encompass both crude dye preparations a well as ammonium salts thereof. The specification, however, does not reasonably suggest that applicant was in possession of compositions that comprise either crude preparations of dyes or ammonium salts thereof, regardless of their absorbance.

8. While the specification teaches that dyes that have a maximum absorbance from 450 to 570 were evaluated, the data shows that the only reagents actually found suitable were those that

range between 508 and 532. Indeed, the record does not support the position that any dye composition was found suitable where the dye had an absorbance below that of 508 or above 532. While dyes within the range of 450 to 570 may have been eliminated because of aesthetic instead of technical reasons (too yellow/orange or too purple; page 25 of the disclosure), the record also clearly states that others were eliminated because they a) "lacked sufficient solubility," b) created a colored DNA pellet; and/or c) proved to be toxic to the polymerase. The specification dos not reasonably suggest how one of skill in the art would be able to recognize other dyes that would sufficiently soluble, not stain a DNA pellet, and not be toxic to the polymerase. As noted by applicant at page 27, lines 1 3-14, the dyes originally considered were "derived from unrelated applications." Accordingly, there is no common feature that would allow for the skilled artisan to recognize those dye members that fall within the claimed genus of compositions from those dyes that fall without.

9. In Table 1 applicant identifies over 180 red dyes that were evaluated. Table 2 lists 40 anionic dyes that were selected for further study. Upon review of Table 2, only four dyes, Acid Red 4, Acid Red 1, Amaranth, and Acid Violet 5 were found to be suitable. While the specification suggests that other colored dyes may be useful in the claimed reagent, the specification does not provide an adequate written description of reagents that comprise other dyes.

Response to argument

10. At page 7 of the response received 24 May 2004 applicant asserts that their selection of red dyes over any other dye color was done for "aesthetic reasons only" and that "persons of

ordinary skill would have understood that applicants were similarly in possession of other colors."

11. The above argument has been fully considered and has not been found persuasive towards the withdrawal of the rejection. It is noted that the claims are drawn to a reagent, which is a composition of matter that is required to comprise specific elements. The specification teaches clearly, and applicant's argument supports the position that only red dyes were evaluated. Of the 180 dyes evaluated, but 6 were found suitable. With applicant not even testing any other color, or any reason, much less finding alternative dyes reagents that are function, yet not preferred, fails to support the position that applicant was in possession of alternative reagent formulations. It appears that applicant is attempting to satisfy the written description requirement of 35 USC 112, first paragraph, through obviousness. Obviousness, however, cannot be relied upon for satisfaction of the written description requirement. In support of this position, attention is directed to the decision in *University of California v. Eli Lilly and Co.* (Fed. Cir. 1997) 43 USPQ2d at 1405, citing *Lockwood v. American Airlines Inc.* (Fed. Cir. 1997) 41 USPQ2d at 1966:

> Recently, we held that a description which renders obvious a claimed invention is not sufficient to satisfy the written description requirement of that invention.

12. For the above reasons, and in the absence of convincing evidence to the contrary, claims 13-16, 20, 42-47, and 60-65 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement.

Claim Rejections - 35 USC § 103

13. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

14. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

15. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

16. Claims 13-16, 20-22, and 60-65 are rejected under 35 U.S.C. 103(a) as being unpatentable over US Patent 5,928,906 (Köster et al.) in view of US Patent 6,117,986 (Nardone et al.).

17. For purposes of examination the claimed composition has been interpreted as allowing for one or more of the component dyes to be associated with a nucleotide that could also be part of a nucleotide sequence, e.g., a labeled primer. While the claimed composition is defined as being "substantially free of the primer and the nucleic acid polymer template," such does not limit in any way the presence of non-template nucleic acid polymers, including that of primers. In support of this interpretation of the claim attention is directed to the following passage from page 16 of the disclosure:

> Examples of essential reagents which can be combined with loading buffer components to formulate a composition of the present invention are: enzyme, concentrated enzyme buffer (e.g. 10X buffer), a nucleotide or primer reagent in the case of DNA or RNA polymerases, or a coenzyme such as NADPH or ATP. The preferred essential agent for this

18. While the claims are drafted in terms of how the reagent is to be used, it is noted with particularity that the claims are drawn to a reagent, not to a method of using same. Accordingly, the claims have been interpreted as encompassing any composition that meets the minimum requirements for components of the composition. Köster et al., column l 2, disclose a variety of compositions that comprise a tracer dye, and a thermostable DNA polymerase (Taq polymerase). It is noted with particularity that Köster et a1., state that the template is added to this mixture.

19. The dyes described by Köster et al., arc not defined in terms of their being anionic tracer dye, nor are they Acid red 1 or Acid Violet 5.

20. Nardone et al., column 3, disclose their unexpected discovery that dyes bound to mononucleotide precursors (applicant's nucleotide) can be incorporated into primers and that

these synthesized compounds can then be used in amplification reactions. Column 6 that Acid Red 1 and Acid Violet 5 were used to label or trace nucleic acids.

21. It would have been obvious to one of ordinary skill in the art at the time that the invention was made to have used anionic dyes such as Acid red 1 and Acid Violet 5 in the composition of Köster et al., as these anionic tracer dyes were known in the art to enhance nucleic acid assays. In view of the well-developed nature of the art, and the explicit guidance found therein, the ordinary artisan would have been highly motivated and would have had a most reasonable expectation of success.

Response to argument

22. At page 11 of the response applicant asserts that claim 60 is free of the above rejection as "[t]he reagent comprises the thermostable DNA polymerase, the detectible anionic tracer dye, and the solute but being ***free of the primer and the nucleic acid polymer template, the reagent having an optical density of about 5 to about 500*** at a visible wavelength of maximal tracer absorbance and a physical density of at least about 1.01 gm/cm^3, but less than the density of the solute" (emphasis in the original).

23. The above argument is not persuasive, as applicant is arguing limitations not present in the claim. It is noted with particularity that claim 60 only requires that the reagent be "substantially free of the primer and the nucleic acid polymer template," which is different from being "free" or primer and template.

24. While the claims recite certain optical densities, or ranges of same, such are not considered to provide a patentable distinction. It is well settled that routine optimization is not patentable, even if it results in significant improvements over the prior art. In support of this

position, attention is directed to the decision in *In re Aller, Lacey, and Hall*, 105 USPQ 233 (CCPA 1955):

> Normally, it is to be expected that a change in temperature, or in concentration, or in both, would be an unpatentable modification. Under some circumstances, however, changes such as these may impart patentability to a process if the particular ranges claimed produce a new and unexpected result which is different in kind and not merely in degree from the results of the prior art. In re Dreyfus, 22 C.C.P.A. (Patents) 830, 73 F.2d 931, 24 USPQ 52; In re Waite et al., 35 C.C.P.A. (Patents) 1117, 168 F.2d 104, 77 USPQ 586. Such ranges are termed "critical" ranges, and the applicant has the burden of proving such criticality. In re Swenson et al., 30 C.C.P.A. (Patents) 809, 132 F.2d 1020, 56 USPQ 372; In re Scherl, 33 C.C.P.A. (Patents) 1193, 156 F.2d 72, 70 USPQ 204. However, even though applicant's modification results in great improvement and utility over the prior art, it may still not be patentable if the modification was within the capabilities of one skilled in the art. In re Sola, 22 C.C.P.A. (Patents) 1313, 77 F.2d 627, 25 USPQ 433; In re Normann et al., 32 C.C.P.A. (Patents) 1248, 150 F.2d 708, 66 USPQ 308; In re Irmscher, 32 C.C.P.A. (Patents) 1259, 150 F.2d 705, 66 USPQ 314. More particularly, where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation. In re Swain et al., 33 C.C.P.A. (Patents) 1250, 156 F.2d 239, 70 USPQ 412; Minnesota Mining and Mfg. Co. v. Coe, 69 App. D.C. 217, 99 F.2d 986, 38 USPQ 213; Allen et al. v. Coe, 77 App. D. C. 324, 135 F.2d 11, 57 USPQ 136. (Emphasis added)

25. For the above reasons, and in the absence of convincing evidence to the contrary, claims 13-16, 20-22, and 60-65 are rejected under 35 U.S.C. 103(a) as being unpatentable over US Patent 5,928,906 (Köster et al.) in view of US Patent 6,117,986 (Nardone et al.).

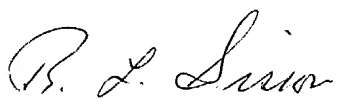
Conclusion

26. Claims 48-53 are allowed.

27. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bradley L. Sisson whose telephone number is (571) 272-0751. The examiner can normally be reached on 6:30 a.m. to 5 p.m., Monday through Thursday.

28. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (571) 272-0782. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

29. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



Bradley L. Sisson
Primary Examiner
Art Unit 1634

BLS
09 August 2004